February 21, 2003

Philip Morris USA
Attn: Research & Development Door 17, Bettie Nelson
615 Maury Street
Richmond, VA 23224

Dear Ms. Nelson:

I have reviewed your e-mail from February 5, 2003 and would like to address several issues.

Issue 1: Focus on the recruitment of the remaining numbers for the no-smoking group on males with low BMI (less than normal) at each of the age categories.

Response: This can be done with a special ad designed to capture this group. Though the call center will collect the height and weight, if the subject is not accurate on these measurements, he may end up in the higher BMI range. We have put into place that the BMI is included on the schedule form that is sent to the sites and the site has been instructed to get height and weight before anything else is done to determine eligibility. The call center is also telling the potential subjects that if they are not accurate, they may not qualify. This should weed out most of the wrong BMI type but if a calculation is in error from the site the subject may still be entered. Doing this will over enroll the non-smoking level cap of 1000. What number, at a minimum, do you want the cells to fill to? 84 is currently the target for each cell.

Issue 2: Please emphasize to all sites the importance of recruiting at least one person in each cell. Several of the sites have empty cells. All of the sites have at least one cell with no subject enrolled.

Response: Several sites are closed and it will be near to impossible to open them back up as the topography devices have already been collected and sent to MDS for additional studies. Sites may not be able to find subjects in each of the cells. Doing this will cause of change in scope, additional costs and more advertising dollars will need to be allocated. This might also cause some sites to drop out of the study, as many of the sites resources will need to be used to try to find the "needle in a haystack". It will also cause over enrollment in some of the tar levels and possibly a need to return to the IRB with an amendment to the protocol for going over the 1000 non-smokers as outlined in the protocol.

Issue 3: In the event that #2 are not done, we will need to determine post-hoc how we wish to handle sites in the analysis. If need be, we would need to collapse the sites in some meaningful way (urban/rural, industrial/non-industrial, etc). We seek your input as to what may make sense with the sites that we have.

Response: I think your statisticians on the data analysis best answer this.

Source: https://www.industrydocuments.ucsf.edu/docs/jglj0001

To re-iterate, changing the stratification now will cause a change in scope and additional costs. We will wait for authorization of the scope change with additional costings before this new stratification is implemented.

Sincerely,

Mary Larson, RN, BSN, CCRC,CCRP
Senior Project Manager
Covance Clinical Research Unit

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